Adipogenesis and epicardial adipose tissue: a novel fate of the epicardium induced by mesenchymal transformation and PPARgamma activation.

Journal: Proc Natl Acad Sci U S A

Publication Year: 2015

Authors: Yukiko Yamaguchi, Susana Cavallero, Michaela Patterson, Hua Shen, Jian Xu, S Ram Kumar, Henry M Sucov

PubMed link: 25646471

Funding Grants: CIRM Stem Cell Biology Training Program

Public Summary:
The adult hearts of most mammals have a substantial amount of fat, but in rodents there is almost none. Thus, the origins and functions of cardiac fat have mostly been unstudied. Here, we demonstrated that the epicardium, the outer cell layer of the heart, is the source of fat in the mammalian heart. We also explained why there is so much in human hearts, and so little in mouse hearts, and showed that the mouse heart can be induced to make more fat by adjusting two specific cellular processes.

Scientific Abstract:
The hearts of many mammalian species are surrounded by an extensive layer of fat called epicardial adipose tissue (EAT). The lineage origins and determinative mechanisms of EAT development are unclear, in part because mice and other experimentally tractable model organisms are thought to not have this tissue. In this study, we show that mouse hearts have EAT, localized to a specific region in the atrial-ventricular groove. Lineage analysis indicates that this adipose tissue originates from the epicardium, a multipotent epithelium that until now is only established to normally generate cardiac fibroblasts and coronary smooth muscle cells. We show that adoption of the adipocyte fate in vivo requires activation of the peroxisome proliferator activated receptor gamma (PPARgamma) pathway, and that this fate can be ectopically induced in mouse ventricular epicardium, either in embryonic or adult stages, by expression and activation of PPARgamma at times of epicardium-mesenchymal transformation. Human embryonic ventricular epicardial cells natively express PPARgamma, which explains the abundant presence of fat seen in human hearts at birth and throughout life.